REMARKS

Claims 1, 12, 23, 26, 38, 47-53, and 55-56 are pending. Claims 2-11, 13-22, 24-25, 27-37, 39-46, and 54 are canceled.

1. In the Advisory Action dated April 8, 2008, it is noted that the 35 U.S.C. 112, second paragraph, rejection was withdrawn. Applicants appreciate Examiner Prebilic's consideration of Applicants' remarks with respect to the 35 U.S.C 112, second paragraph rejection.

2. In the Final Office Action, claims 1, 12, 23, 26, 38, 47-53, and 55-56 were rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. Applicants respectfully traverse this rejection.

Specifically, the PTO states that the present claims contain "subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claimed hydroxyapatite to tricalcium phosphate ratios lack original support from the specification in that the ratios originally provided were for sintered pure hydroxyapatite and not the hydroxyapatite stabilized with stabilizing entities as presently claimed." (Final Office Action, pg. 2).

The originally filed application indeed discloses and fully conveys that the inventors had possession of the compositional range of 50:50 to 80:20 stabilized alpha tricalcium phosphate to hydroxyapatite in connection with stabilized alpha tricalcium phosphate. Applicants point out that the original disclosure includes not only the description and drawings as filed, but also the original claims. (MPEP 608.01(l)). In particular, the original claims 11 and 21, which include the subject matter of the base claims 1 and 13, respectively, unequivocally disclose the claimed ratios in relation to *stabilized* calcium phosphate phases. Original claims 1, 11, 13, and 21 are reproduced below for convenience (emphasis added).

1. A bioactive artificial sintered composition for providing a morphology capable of consistently supporting bone cell activity thereon, said composition comprising stabilized calcium phosphate phases developed by the conversion of a hydroxyapatite substance in the presence of stabilizing entities at sintering temperatures into insolubilized and stabilized tricalcium phosphate.

11. A composition as claimed in claim 1, wherein said calcium phosphate phases are in a ratio of 50:50 to 20:80 for hydroxyapatite to alpha tricalcium phosphate.

13. A process for stabilizing an artificial sintered composition of calcium phosphate phases having a morphology suitable for supporting bone cell activity thereon, said process comprising converting a hydroxyapatite substance, into primarily alpha tricalcium phosphate by sintering, and providing stabilizing entities which stabilize and insolubilize the formed alpha tricalcium phosphate within the phosphate phases.

21. A process as claimed in claim 13, wherein said calcium phosphate phases are in a ratio of 50:50 to 20:80 for the ratio of hydroxyapatite to alpha tricalcium phosphate.

Original claims 11 and 21 clearly associate stabilized calcium phosphate phases with the ratio of hydroxyapatite to alpha tricalcium phosphate. Because the original claims 11 and 21 have been canceled, Applicants have amended the specification to reflect the subject matter of the originally submitted claims and have added paragraphs to the Summary of the Invention section that include the precise language of claims 1, 11, 13, and 21, to provide antecedent basis for the claimed subject matter.

The description as originally filed even further supports Applicants' position that the claimed subject matter is fully compliant with 35 U.S.C. 112, first paragraph. The original description, page 9, under Detailed Description of the Preferred Embodiments, states that the composition of the present calcium phosphate substance is provided in Applicants' prior work

focused on pure HA, which has a HA:alpha-TCP ratio within clearly stated desired ratios of 50:50 to 80:20. Although the claimed invention is directed to a modified composition relative to pure HA, which composition is stabilized and thus bioactive to support osteoblastic bone growth and to support extracellular resorption of the composition by osteoclasts, the compositional features of Applicants' prior work on pure HA remains applicable to the presently claimed compositions.

The foregoing nexus with Applicants' prior work is quite clear when the originally filed application is viewed in its entirety, including the original claims as noted above, and further, description in the specification clearly linking the desired ratios to stabilized materials of the claimed invention. More specifically, the desired ratios of HA:alpha-TCP are disclosed in connection with the embodiment in Procedure 7, page 32, lines 22-23. Here, it is additionally pointed out that the disclosure of desired ratios in connection with Procedure 7 is made with respect to choosing sintering temperatures, clearly linking the desired ratios of Applicant's prior work in the paragraph bridging pages 12 and 13 with stabilized embodiments. That is, in both Applicants' prior work and present invention, sintering temperatures are chosen to manifest the desired ratios as claimed.

Briefly summarizing, the clear language of the original claims clearly provides 35 U.S.C. 112, first paragraph support for the claimed subject matter, and that support is further bolstered by the clear intent of the original description that the compositional features of Applicants' prior work on pure HA are applicable to the claimed invention.

For at least the foregoing reasons, Applicants respectfully submit that the subject matter of the claims is describe in such a way as to convey to one skilled in the bone replacement ceramic arts that the inventors, at the time the application was filed, had possession of the claimed invention. As such, Applicants respectfully request reconsideration and withdrawal of the 35 U.S.C. 112, first paragraph, rejection.

3. Claims 1, 12, 23, 26, 38, and 47 were rejected under 35 U.S.C. 102(b) as being anticipated by Ruys (article entitled "Silicon-doped hydroxyapatite") or, in the alternative under 35 U.S.C. 103(a) as obvious over Ruys alone, and claims 48-53 and 55-56 were rejected under

35 U.S.C. 103(a) as being upatentable over Ruys alone. Applicants respectfully traverse these rejections.

Present claim 1 is directed to a bioactive artificial sintered composition for supporting bone selectivity. The composition consists essentially of stabilized alpha tricalcium phosphate and hydroxyapatite at a ratio of at least 50:50 alpha tricalcium phosphate: hydroxyapatite. The stabilized alpha tricalcium phosphate is stabilized with a stabilizing entity selected from the group consisting of silicon entities, aluminum entities, barium entities, titanium entities, germanium entities, chromium entities, vanadium entities, niobium entities, boron entities, and mixtures thereof. The composition is bioactive to support osteoblast bone growth and to support extracellular resorption of the composition by osteoclasts.

Present claim 50 is directed to a bone replacement composition comprising alpha tricalcium phosphate and hydroxyapatite in a ratio of at least 666:333 alpha tricalcium phosphate to hydroxyapatite. The alpha tricalcium phosphate is stabilized with a stabilizing entity selected from the group consisting of silicon entities, aluminum entities, barium entities, titanium entities, germanium entities, chromium entities, vanadium entities, niobium entities, boron entities, and mixtures thereof.

Present claim 55 is directed to a bioactive artificial sintered composition for supporting bone cell activity. The composition includes a stabilized alpha tricalcium phosphate and hydroxyapatite in a ratio of at least 666:333 alpha tricalcium phosphate to hydroxyapatite. The stabilized alpha tricalcium phosphate is stabilized with a stabilizing entity selected from a group consisting of silicon, aluminum, barium, titanium, germanium, chromium, vanadium, niobium, boron and mixtures thereof. The composition is insoluble in physiological fluids of pH 6.4 to 7.3. The composition is bioactive to support osteoblast bone growth and to support extracellular resorption of the composition by osteoclasts.

Turning to the reference, Ruys presented work to determine the feasibility of chemically doping hydroxyapatite with silicon. At all silicon levels hydroxyapatite (HAp) formed and, at high silicon levels, α-tricalcium phosphate (α-TCP) and Si-P-O glass formed. (Ruys, Abstract). In particular, "both α- and β-TCP were formed, although β-TCP was favoured at low silicon levels and α-TCP was favoured at high silicon levels. Further, at higher silicon concentrations, a

broad X-ray diffraction peak with a *d* spacing of 0.16-0.26 nm formed. Since both silicon and phosphorous are oxide glass formers, this peak is a result of the presence of a Si-P-O glass. For progressively higher silicon levels, the glass became the dominant phase. At very high dopant levels, approximate area ratios of the main diffraction peaks of HAp and TCP suggested that the TCP content was slightly greater than the HAp content." (Ruys, page 77, paragraph 3). As such, Ruys discloses that at high silicon levels the TCP content was slightly greater than hydroxyapatite content, but the Si-P-O glass phase was the dominant phase.

High levels of Si-P-O glass and in particular, high levels of silicon outside of the crystal matrix of the calcium phosphate species hinder the bioactivity of the material. As described in the Declaration by Dr. Smith dated November 2, 2007, high levels of silicon produce a material that limits initial cell attachment to the surface. In addition, a cited impartial third party reference clearly states that high levels of silicon inhibit osteoclast activity. (See Best et al. pg. 986). Thus, high levels of silicon, which, as taught by Ruys, leads to the formation of Si-P-O glass as a dominant phase, materially affects the bioactivity of the material in that it inhibits osteoclast activity.

With regard to claim 1, Applicants have used the transitional phrase "consisting essentially of," which limits the scope of a claim to the specific materials or steps and those that do not materially affect the basic and novel characteristics of the claimed invention. Clearly, the compositions disclosed by Ruys have a predominant phase of Si-P-O glass for any embodiment having notable α-TCP content, materially affecting the basic and novel characteristics of the claimed invention, namely bioactivity, including osteoclast activity. The PTO is directed to MPEP 2111.03, which is instructive on issues relating to interpretation of "consisting essentially of" language. That section makes clear that Applicants have the burden to establish the identity of basic and novel characteristics; otherwise "consisting essentially of" shall be construed by the PTO to be "comprising." However, Applicants have met this burden by (i) actually *claiming* one of the basic and novel characteristics (i.e., the composition is bioactive), and (ii) providing impartial third party evidence that high silicon content, which Ruys states leads to a predominant glass phase, hinders bioactivity (i.e., see Best et al., pg. 986). Interestingly, the MPEP chose to cite *In re Janakirama-Rao* (137 USPQ 893, 895-96 (CCPA 1963)) involving facts similar to

those at hand, in which excessive silicon content was precluded by consisting essentially of language, based on evidence of deleterious affects of silicone content greater than 0.5 wt%.

The Ruys material does not *consist essentially of* a bioactive, high α-TCP content material since the high α-TCP-content materials of Ruys contain notable Si-P-O glass, significantly compromising the bioactivity of the material in terms of osteoclast activity. In this regard and as noted in the Declaration by Dr. Smith dated November 2, 2007, Applicants have found that external Si-containing phases, such as Si-P-O glass, in amounts greater than 20 wt% compromise bioactivity as claimed, that is, "to support osteoblastic bone growth and to support extracellular resorption of said composition by osteoclasts."

In contrast to Ruys, Applicants have discovered a method for producing bone replacement compositions predominantly formed of stabilized calcium phosphate phases without the formation of a significant amount of silicon compounds outside of the calcium phosphate matrices. As noted in the Declaration, the method is significantly different from the method disclosed in Ruys, and the material produced by such a method is different from the material disclosed by Ruys. In particular, the compositions produced by the methods discovered by Applicants are predominantly calcium phosphate compositions and have less than 5 wt% of phases including silicon compounds other than silicon stabilized calcium phosphate compositions, such as less than about 3 wt% silicon compound phases. As further explained in the Declaration, the absence of a significant amount of silicon compositions other than the silicon stabilized calcium phosphate compounds in the presence of stabilized α-TCP permits bioactivity and, in particular, permits balanced osteoblast and osteoclast activity as claimed.

Accordingly, based on the transitional phrase "consisting essentially of," claim 1 clearly precludes the presence of Si-P-O glass in amounts over 20 wt%, and certainly as a "predominant phase" as taught by Ruys. As such, Ruys fails to anticipate claim 1 and claim 1 is not obvious over Ruys because the high TCP content materials of Ruys include Si-P-O glass as a predominant phase.

With respect to claim 12, Applicants have presented evidence above and in previous responses that Ruys fails to inherently disclose the claimed features.

Turning to independent claims 50 and 55, both claims recite a composition comprising alpha tricalcium phosphate and hydroxyapatite in a ratio of at least 666:333 alpha tricalcium phosphate to hydroxyapatite. In particular, claim 50 relates to a bulk bone replacement composition having the above ratio of calcium phosphate species. Ruys is clearly limited to, at best, TCP content "slightly greater" than the HAp content. A ratio of 666:333 is clearly greater than any ratio fairly derived from the teachings of Ruys.

With respect to Ruys, the PTO asserts that since low dopant levels are only preferred and the concept of high dopant levels is also disclosed, it would have been obvious to make higher dopant materials that would fall within the claimed range. However, Ruys teaches consistently throughout the reference against the formation of materials with high TCP content. For example, on page 71, Ruys states that particular mole ratios should be used "in order to avoid formation of biodegradable TCP (emphasis added)." On page 74 in the last paragraph, Ruys teaches use of stir/boil methods "in order to eliminate TCP from the calcined product (emphasis added)." Further, Ruys teaches on page 77, second paragraph that "TCP is an undesirable phase ... (emphasis added)."

Clearly, Ruys teaches away from the formation of materials that include TCP. As such, one skilled in the bone replacement arts would have been deterred from forming compositions having at least 666:333 stabilized tricalcium phosphate to hydroxyapatite and thus, would not have been motivated to form such a composition.

For at least the foregoing reasons, claims 1, 12, 23, 38, 47-53, and 55-56 are not anticipated by and are patentable over Ruys. As such, Applicants respectfully request reconsideration and withdrawal of the 35 U.S.C. 102(b) rejection and 35 U.S.C. 103(a) rejection of claims 1, 12, 23, 38, and 47 and respectfully request reconsideration and withdrawal of the 35 U.S.C. 103(a) rejection of claims 48-53 and 55-56.

4. Applicants would like to further clarify the Declaration provided by Dr. Smith. As mentioned during the telephonic interview, Applicants attempted to reproduce the data provided by Ruys by following the experimental procedure outlined by Ruys. Despite a faithful attempt to follow the method steps outlined in Ruys, Applicants were unable to synthesize the hydroxyapatite sample Ruys purportedly formed through the method on page 74. Specifically,

Applicants were unable to produce hydroxyapatite material free of tricalcium phosphate phases using the method disclosed by Ruys. Since this material was a starting material used in forming the rest of the materials of Ruys, the inability to produce such a material would lead to errors if the remaining steps were performed. As such, steps or parameters key to the formation of the samples of Ruys may not have been disclosed in the reference, meaning Ruys is not enabled.

Because Applicants were unable to reproduce the materials of Ruys through the methods disclosed by Ruys, Dr. Smith outlined differences between the methods of the present application and that of Ruys. Such differences may explain why Ruys did not produce the claimed materials and thus, provide evidence as to why the claimed materials are not inherently disclosed by Ruys. Further, Dr. Smith provided impartial third party references in support of the position that the material of Ruys is not bioactive as defined in the present specification and claims.

5. As requested by the PTO, Applicants have disclosed to the PTO the existence of copending Patent Application No. 11/738,052 in an Information Disclosure Statement filed November 2, 2007. In addition, Applicants requested reissue of US 6,323,146 on January 30, 2008, which issued from a continuation-in-part application claiming priority to the present application.

Applicant(s) respectfully submit that the present application is now in condition for allowance. Accordingly, the Examiner is requested to issue a Notice of Allowance for all pending claims.

Should the Examiner deem that any further action by the Applicants would be desirable for placing this application in even better condition for issue, the Examiner is requested to telephone Applicants' undersigned representative at the number listed below.

The Commissioner is hereby authorized to charge any fees, which may be required, or credit any overpayment, to Deposit Account Number 50-3797.

Respectfully submitted,

4.15.08
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